REMARKS

This document is filed in reply to the office action dated March 13, 2003 ("Office Action") and the Notice of Draftsperson's Patent Drawing Review dated March 6, 2003.

Applicants submit herewith formal drawings as required by 37 CFR §1.84 and 1.152.

Applicants have added claim 31, support of which appears at page 2, lines 29-30. Applicants have amended claim 14 to recite three steps of the claimed method. Support for the recited three steps can be found at page 10, line 14 through page 11, line 2 and in original claim 30. Applicants have also amended the Specification at the Examiner's request to delete embedded hyperlinks. No new matter has been introduced.

Claims 1-31 are pending. Claims 3-13 and 15-30, drawn to non-elected inventions, have been withdrawn. Claims 1, 2, and 14 have been examined. Reconsideration of these claims and claim 31 are respectfully requested.

Objection against the Specification

The Examiner objected to the Specification for containing embedded hyperlinks. See the Office Action, page 3, part 4. Applicants submit that the ground for objection has been overcome by the above amendments.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1 and 14 for being indefinite. It is the Examiner's position that the claims "omit[ ] essential steps ... to detect the absence or presence of [a] superantigen." See Office Action, page 4, part 5.

Applicants have amended claim 14 to recite three essential steps. These amendments are believed to have overcome the ground for rejection against this claim. As to claim 1, Applicants would like to point out that this claim, drawn to a superantigen, does not cover a detection method and therefore does not need to recite steps of a detection method.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner further rejected claims 1, 2, and 14 for lack of enablement. See the Office Action, page 3, part 6. More specifically, the Examiner stated that "the specification, while being enabled for a superantigen SMEZ-2, ... does not reasonably provide enablement for" its functionally equivalent variants. To support this statement, the Examiner cites five references, i.e., Burgess et al., Lazar et al., Bowie et al., Kumar et al., and Houghten et al., which respectively discuss the effects of certain point mutations in acidic FGF, TGFα, lac repressor, Myelin Basic Protein, and the influenza hemagglutinin protein. Some of these mutations reduce or abolish activities of the proteins, while others do not. The Examiner notes that "[t]hese references demonstrate that even a single amino acid substitution ... will often dramatically affect the biological activity of a protein," and concluded that undue experimentation would be required to enable the full scope of the claims. Applicants respectfully traverse.

Applicants agree that it is possible to abolish activity of a given protein by mutating a critical residue, as disclosed by the five cited references. However, Applicants disagree that this fact means that one of ordinary skill cannot make functional equivalent variants of SMEZ-2 without undue experimentation.

In fact, Bowie et al. teaches, at page 1306, col.2, lines 12-13, that "proteins are surprisingly tolerant of amino acid substitutions." Bowie et al. cites as evidence a study carried out on the *lac* repressor. Of approximately 1500 single amino acid substitutions at 142 positions in this protein, about one-half of the substitutions were found to be "phenotypically silent," i.e., exerting no noticeable effect on the activity of the protein (page 1306, col. 2, lines 14-17). Presumably, the other half of the substitutions exhibited effects ranging from slight to complete abolishment of repressor activity. Thus, one can expect, based on Bowie et al.'s teachings, to find over half (and possibly well over half) of random substitutions in any given protein to result in mutated proteins with some or full activity. These are far better odds than those at issue in *In re Wands,* 858 F.2d 731 (Fed. Cir. 1988), in which the court said that screening a large number of hybridomas to find the few that fell within the claims was not undue experimentation. The question is not whether it is possible to abolish activity with a point mutation (as the Examiner seems to believe), but rather whether one of ordinary skill can produce, without undue

experimentation, variants in which the activity is not abolished. Based on Bowie et al.'s teachings, one would predict that even random substitutions of residues in SMEZ-2 will predictably result in a majority of the variants' having full or partial activity. Given the information provided in the specification regarding conserved residues in SMEZ-2 (see Fig. 1 and page 6, lines 9-30), one skilled in the art would know to avoid those residues or make only conservative changes, thereby achieving a high success rate.

Furthermore, the specification amply teaches how to make and test variants to find those with the SMEZ-2 activity required by the claims. See, page 9, last paragraph, and pages 16-17, respectively.

In view of the above remarks, Applicants request withdrawal of the rejection for lack of enablement.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejected claims 1 and 2 as being anticipated by Kamezawa et al. ("Kamezawa"). See the Office Action, page 9, part 8. According to the Examiner, Kamezawa teaches an SMEZ superantigen that "appears to be the same as claimed ... [and] to have the same functions." See the Office Action, page 9, lines 12-14.

Applicants disagree. Claim 1 covers a superantigen selected from SMEZ-2, SPE-G, SPE-H, and SPE-J, or their functionally equivalent variants. Claim 2 covers a superantigen SMEZ-2 that has the amino acid sequence of SEQ ID NO: 2, or its functionally equivalent variant. In Fig. 1 of the Specification, Applicants have aligned the sequence of SMEZ-2 ("SMEZ-2") against the sequence of SMEZ taught in Kamezawa ("SMEZ"). These two sequences differ in 17 amino acid residues. See page 5, lines 17-23. Further, these two superantigens also differ in their potencies to stimulate peripheral blood lymphocytes, specificities to enrich TcR Vβ, and abilities to bind MHC class II molecules. See Tables 1, 2, and 3, respectively. Clearly, contrary to the Examiner's assertion, SMEZ taught in Kamezawa differs from SMEZ-2 covered by claims 1 and 2. Thus, Kamezawa does not anticipate these two claims.

CONCLUSION

For the above remarks, Applicants submit that the grounds for rejection asserted by the Examiner have been overcome, and the claims, as pending, define subject matter that is definite, enabled, and novel. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Please apply any other charges to deposit account 06-1050, referencing attorney docket 12669-003US1.

Respectfully submitted,

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